Giant cell arteritis, truly a form of systemic vasculitis

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EDITORIAL

Giant cell arteritis, truly a form of systemic vasculitis

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Giant cell arteritis (GCA) was first described as a temporal arteritis by Horton, Magath and Brown in 1932, but Cooke et al. already demonstrated in 1945 by autopsy that it could be a generalised vasculitis of the aorta and its main branches.[1] In fact, Cooke recognised that in the elderly 'a widespread arterial disease existed, not uncommon but rarely recognised'. Moreover he stated that the term temporal arteritis has been retained to indicate a specific clinical entity in the absence of any definite aetiological factor. Nowadays, with the availability of modern age imaging (ultrasound, PET-CT, CTA, MRA,) the awareness of extracranial GCA has risen significantly. GCA is the most prevalent form of systemic vasculitis, especially in ageing Caucasian populations.[2]

Lensen et al. wrote an elaborate narrative review on extracranial GCA.[3] It is apparent that a clear consensus on the best diagnostic imaging modality is lacking and that the diagnosis is usually based on the clinical signs and symptoms together with the locally available imaging modalities and expertise. Also, they point out that evidence-based treatment guidelines are lacking and that the same treatment regimen for cranial and non-cranial GCA is applied. Moreover, it is unclear what the best strategy is to monitor disease activity and how to deal with relapsing patients. The latter is a clear problem since up to 64% of patients with GCA experience a relapse.[4] Part of the lack of knowledge and/or consensus might be due to the high variability in presenting clinical symptoms, from headache to night sweats and polymyalgia rheumatica like symptoms, as well as the associated dispersion over many different medical specialists, including general practitioners, neurologists, ophthalmologists, internists, rheumatologists, and vascular surgeons. It is increasingly recognised that GCA is a debilitating disease, which causes significant morbidity in otherwise healthy 50+ persons, not in the least due to the long-term use of glucocorticoids.

Improving outcome has to start with early and timely recognition of patients presenting with GCA. Especially cranial GCA symptoms are linked to irreversible loss of vision and this could be prevented by early aggressive treatment with steroids.[5] Also, the recognition of aortic structural damage including aneurysm development is of importance. However, long-term incidence and the relative contribution of atherosclerotic and inflammatory components are unclear and better studies are needed.

Fast-track clinical pathways have been established in several specialist centres, providing initial diagnostic evaluation and treatment of patients with suspected GCA within 24 hours. Preliminary results suggest a significant reduction of permanent visual impairment compared with conventional referral strategies.[6]
Another important issue that needs to be addressed is increasing public and general practitioner awareness of GCA as a debilitating disease in order to reduce the referral time to the fast track clinic.

Ideally a fixed work-up protocol with standardised and validated lab and imaging techniques should be available in a day-care setting. In such a setup, ultrasound is a promising tool, and not only for cranial GCA, as it is easily accessible and relatively inexpensive in contrast to more advanced imaging strategies. Since the landmark study by Schmidt in 1997,[7] several studies on the use of Duplex ultrasound (combination of colour Doppler and pulsed-wave-Doppler) in the diagnosis and follow-up of cranial GCA have been published. In addition to early detection of stenosis and occlusion, a typical dark hypoechoic, circumferential wall thickening is usually observed in a vessel affected by vasculitis, referred to as the 'halo' sign. For cranial GCA, the accuracy has been tested in several studies, using histological diagnosis as the gold standard, yielding good sensitivity, specificity, and reproducibility when performed by

experienced sonographers. Preliminary results from the recently completed prospective multicentre TABUL study (Temporal Artery Biopsy vs Ultrasound in diagnosis of GCA; NCT00974883) including 415 cases with suspected cranial GCA suggests that ultrasound is only of diagnostic value if performed within four days of steroid initiation as the typical halo quickly diminished over time. Of importance, these typical ultrasound signs can also be observed in patients with extracranial GCA, predominantly affecting axillary, subclavian and/or proximal brachial arteries. Clinical cohorts have suggested that the axillary artery may be very useful and is generally found to be affected in most cases of extracranial GCA.[8] However, contrary to temporal ultrasound, it is not possible to use histology as a gold standard and no formal validation study has been performed.

Treatment should be started promptly in GCA patients with cranial symptoms, but can probably be delayed in extracranial GCA in order to make the proper diagnosis. Whether aggressive treatment also leads to a decrease in long-term aortic structural damage is as yet unclear.
Imaging studies clearly show that the inflammatory signal rapidly decreases after starting glucocorticoids. Treatment is still based largely on glucocorticoids monotherapy, but the disease-modifying antirheumatic drugs methotrexate, lefunomide, azathioprine and a very recently published randomised controlled trial (RCT) in 30 patients with tocilizumab, an IL6-receptor blocking biological,[9] have demonstrated varying benefits. The results of the much larger international four arm double-blinded RCT with tocilizumab and different steroid-tapering regimens (GiACTA, NCT01791153) are awaited soon.

In summary, Lensen et al. highlight a number of challenges in extracranial GCA and new developments give us hope that it will not take another 70 years to solve the areas of uncertainty presented in their discussion.

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